UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

December 10, 2002

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: Secondary Review of Contractor's (DynoCorp I & ET) Efficacy Review of Anthium Dioxcide 5% Aqueous Stabilized Chlorine Dioxide,
EPA Reg. No. 9150-2
Case No. 023044
DP Barcode: D284432

From: Bruce H. Mann
Efficacy Evaluation Team
Product Science Branch (7510C)

To: Robert Brennis, PM 32/Wanda Mitchell
Regulatory Management Team II
Antimicrobials Division (7510C)

Thru: Emily Mitchell, M.S., Team Leader Emily Mitchell 12-19-02
Efficacy Evaluation
Product Science Branch

Applicant: International Dioxcide, Inc.
554 Ten Rod Road
North Kingstown, Rhode Island 02852

Formulation Label:

Active Ingredient(s)	% by wt.
Chlorine Dioxide	5.00
Inert Ingredient(s)	95.00
Total	100.00

I BACKGROUND

The product, Anthium Dioxcide (EPA Reg. No. 9150-2), is an Agency-approved disinfectant, deodorizer, slimicide, and food-contact surface sanitizer for use on hard, non-porous surfaces in industrial and institutional environments. The applicant requested an amendment to the registration of this product to add claims for effectiveness against additional microorganisms, specifically foot-and-mouth disease virus, swine flu virus, and African swine fever virus. The proposed label does not identify any specific bacteria or viruses. The study was conducted at the USDA Foreign Animal Disease Diagnostic Laboratory in Greenport, New York.

This data package contained one study (MRID No. 457142-01), a Statement of No Data Confidentiality, and the last accepted label dated 09-20-2000.

II USE DIRECTIONS

The product is designed to be used for disinfecting non-porous, hard surfaces such as tile floors, walls, ceilings, stainless steel cold rooms, walk-in incubators, bench tops, biological hoods, incubators, stainless steel equipment and instruments, water bath incubators, and water storage systems (e.g., water storage systems aboard aircraft, boats, recreational vehicles, off-shore drilling rigs). The proposed label directions provide the following information regarding preparation and use of the product as a disinfectant: Thoroughly clean all surfaces with soap. In a well-ventilated area, prepare an activated use solution by placing the specified amount [see below] of the product into a clean, plastic pail; and adding the specified amount [see below] of clean potable water and Activator-C. Let the use solution stand for 15 minutes and let the activator dissolve completely. As an alternate activation method, the pH may be adjusted using acetic, citric, phosphoric, sulfuric, or hydrochloric acid, or Activator K. An activated use solution can also be prepared electrolytically by adding the product directly to the Oxychlor e-generator.

Intended Use and Contact Time	Preparation of Use Solution	Dilution
Disinfectant for tile floors, walls, ceilings, stainless steel cold rooms, and walk-in incubators; and for water bath incubators Contact Time: 10 minutes; 1 hour for disinfecting water bath incubators	0.8 ounces product 1 gallon of water 1.2 grams of Activator-C (300 ppm available chlorine dioxide according to the proposed label)	1:160

Intended Use and Contact Time	Preparation of Use Solution	Dilution
Disinfectant for bench tops, biological hoods, incubators, stainless steel equipment and instruments. Contact Time: 10 minutes	10 mL of product 1 L of water 0.3 grams of Activator-C (300 ppm available chlorine dioxide according to the proposed label; 500 ppm available chlorine according to the last accepted label)	1:100
Disinfectant for commercial animal confinement facilities (e.g., poultry houses, swine pens, calf barns, kennels) Contact Time: Not specified; a portion of proposed label is "blank". Last accepted label specifies a contact time of 10 minutes	1 1/3 fl. oz. product 1 gallon of water 1.2 grams of Activator-C (300 ppm available chlorine dioxide according to the proposed label; 500 ppm available chlorine according to the last accepted label)	1:96
Disinfectant for water storage systems aboard aircraft, boats, recreational vehicles, off-shore oil rigs, etc. Contact Time: 10 minutes or 1 hour	For 10-minute procedure: same dilution as above. For 1-hour procedure: 1 1/3 fl. oz. product 10 gallons of water 1.2 grams of Activator-C (apparently 50 ppm available chlorine dioxide)	1:960

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Virucides

The effectiveness of virucides against specific viruses must be supported by efficacy data that simulates, to the extent possible in the laboratory, the conditions under which the product is intended to be used. Carrier methods that are modifications of either the AOAC Use-Dilution Method (for liquid disinfectants) or the AOAC Germicidal Spray Products Test (for spray disinfectants) must be used in developing data for virucides intended for use upon dry inanimate, environmental surfaces (e.g., floors, tables, cleaned dried medical instruments). To simulate in-use conditions, the specific virus to be treated must be inoculated onto hard surfaces, allowed to dry, and then treated with the product according to the directions for use on the product label. One surface for each of two different batches of disinfectant must be tested against a recoverable virus titer of at least 10^4 from the test surface for a specified exposure period at room temperature. Then, the virus must be assayed by an appropriate virological technique. Separate studies are required for each virus. The calculated viral titers must be reported with the test results. For the data to be considered acceptable, results must demonstrate complete inactivation of the virus at all dilutions. When cytotoxicity is evident, at least a 3-log reduction in titer must be demonstrated beyond the cytotoxic level. These Agency standards are presented in DIS/TSS-7. To ensure that a virus protocol has been adequately validated, data should be provided from at least two independent laboratories for each product tested (i.e., two batches per product per laboratory). The validation of a protocol requires the use of two carriers per batch of product as well as the use of a common positive control disinfectant to be tested concurrently with all new products. These Agency standards are

tailored from those presented in the Federal Register, Vol. 65, No. 166, Friday, August 25, 2000.

In future studies, all generated and submitted studies must be provided with a Quality Assurance Unit Statement (QAU) which contain the proper signatures as specified in Section 160.35 (b)(7); and a statement of GLP as specified in Section160.12(a) of 40 CFR.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDY

1. MRID 457142-01 "Efficacy of Anthium Dioxcide Against Selected Foreign Animal Disease Agents," by Carol House. Study conducted at USDA Foreign Animal Disease Diagnostic Laboratory (FADDL). Study completion date – July 14, 1994.

This study was conducted against Foot-and-Mouth Disease Virus (FMDV-O_1 Campos, Sept 91), Swine Vesicular Disease Virus (SVDV-UK 13 Feb 92), and African Swine Fever Virus (ASFV-Brazil, Strain 26 Vero x 178, 2/84). One lot (Lot No. SD-477) of the product, Anthium Dioxcide, was tested according to FADDL Protocol No. 080 (copy provided). The product was diluted 1:140 in water, followed by pH adjustment to 3.0 with citric acid. The solution was allowed to set at room temperature for 15 minutes prior to use, as specified on the product label. [According to FADDL Protocol No. 080, the product is to be tested at 2 times the recommended concentration. It is assumed that the efficacy study conducted was for a 1:70 dilution of the product.]

For the study against Foot-and-Mouth Disease Virus and Swine Vesicular Disease Virus, 0.75 mL of each virus in test medium [concentration not provided] and 0.75 mL of the use solution were mixed and incubated for 5 minutes at 25°C. The test medium was Eagles minimum essential medium [EMEM] with Earle's balanced salt solution, without glutamine, supplemented with 2.5% fetal bovine serum. The virus-test medium-disinfectant mixture (1.5 mL) was poured into prepared Sephadex LH-50 columns; the mixture was centrifuged for 15 minutes at 1000 xg. The fluid collected from each column (referred to as the "surviving virus" in FADDL Protocol No. 080) was titrated using 10-fold dilutions in supplemented EMEM. [Information about the host system and incubation conditions was not provided.] Three sets of replicates were performed on different days, and submitted for statistical analysis. Controls included a virus control and a toxicity control.

For the study against African Swine Fever Virus, primary swine buffy coat cells in a 96-well plate were inoculated with an aliquot (amount not specified; assumed to be 0.025 mL) of each dilution. The plates were incubated 4-6 days at 37°C in a 95% humidified atmosphere of 5% CO_2. The plates were read by shaking slightly to agitate the erythrocytes and reading page 4 of 6 hemagglutination under a microscope. The titer was calculated as $TCID_{50}$/0.025 mL. Three sets of replicates were performed on different days, and submitted for statistical analysis. Information about controls was not provided.

V RESULTS

MRID Number	Organism	Results ($TCID_{50}$/0.025 mL)			Average ($TCID_{50}$/ 0.025 mL)
		Trial A	Trial B	Trial C	
457142-01	Foot-and-Mouth Disease Virus*	$10^{0.0}$	$10^{0.0}$	$10^{0.0}$	$10^{0.0}$
	(Virus Control) (Cytotoxicity Control)	$10^{3.8}$ $10^{3.8}$	$10^{3.2}$ $10^{3.4}$	$10^{3.7}$ $10^{3.7}$	$10^{3.6}$ $10^{3.6}$
457142-01	Swine Vesicular Disease Virus*	$10^{0.7}$	$10^{0.0}$	$10^{0.0}$	$10^{0.2}$
	(VirusControl) (Cytotoxicity Control)	$10^{5.4}$ $10^{5.4}$	$10^{5.1}$ $10^{5.5}$	$10^{5.2}$ $10^{5.3}$	$10^{5.3}$ $10^{5.3}$
457142-01	African Swine Fever Virus**	$10^{0.0}$	$10^{0.0}$	$10^{0.0}$	$10^{0.0}$
	(Virus Control) (Cytotoxicity Control)	$10^{2.5}$ $10^{2.5}$	$10^{2.5}$ $10^{2.5}$	$10^{2.5}$ $10^{2.5}$	$10^{2.5}$ $10^{2.5}$

$10^{0.0}$ denotes that no virus was detected in the undiluted sample.

* Titrations performed using 10 wells/dilution (10^{0} to 10^{-7}).

** Titers expressed as hemugglutination units 50%.

VI CONCLUSIONS

In the three trials conducted with anthium dioxide, the product demonstrated complete inactivation of the Foot and Mouth Disease Virus and the African Swine Fever Virus when tested at 390 ppm chlorine dioxide for 5 minutes at 25°C. Cytotoxicity was not detected in any of the tested samples.

VII RECOMMENDATIONS

The submitted efficacy data (MRID No. 457142-01) could be upgraded for registration of Anthium Dioxcide 5% Aqueous Stabilized Chlorine Dioxide, as a disinfectant with virucidal activity when tested against the microorganisms, Foot-and-Mouth Disease Virus, Swine Vesicular Disease Virus and African Swine Fever Virus in the presence of a 2.5% organic soil load (fetal bovine serum) on hard, non-porous surfaces for a contact time of 5 minutes and at an assumed dilution of 1:70 if another batch of the product was tested under the same conditions as the previous batch, or evidence was submitted that the testing conducted in 1994 was done under Good Laboratory Practices (GLP) against separate batches of the product, and demonstrated complete inactivation of FMDV.